Factors affecting the fetal hemoglobin levels in patients with sickle cell anemia and thalassemia

Stellingen

behorende bij het proefschrift

Factors affecting the fetal hemoglobin levels
in patients with
sickle cell anemia and thalassemia

van

Aleksandar Jovo Dimovski

Maastricht
25 november 1993

1. The polymorphic patterns of the $(AT)_x(T)_y$ repeats at -530 5' to the β-globin gene do not correlate with the level of Hb F in patients with β-thalassemia major.

2. The determination of specific sequence variations in the 5' flanking region of the $^{G}\gamma$- and $^{A}\gamma$-globin genes is a reliable, time- and cost-effective procedure for the determination of the major β^S haplotypes.

3. The **C->T** substitution at position -158 5' to the $^{G}\gamma$ gene is the most consistent sequence variation associated with the β^S and β-thal chromosomes which are capable of conferring high Hb F expression under the hematopoietic stress of these diseases.

4. The possible influence of the sequence variations in the 5' flanking region of the $^{G}\gamma$- and $^{A}\gamma$-globin genes and in the LCR HS-2 on the overall expression of the γ-globin genes should be tested in an experimental system where the conditions of hematopoietic stress could be reproduced, **i.e.** transgenic mice.

5. The silencing effect of the 3' HS-1 sequences should be further evaluated through studies of patients with additional deletions or mutations within this sequence.

6. The improvement in DNA methodology, particularly the PCR-related procedures, makes the determination of various Hb variants by this technique a method of choice when compared to the classical protein chemistry analysis.

7. Gene therapy in hemoglobinopathies is hampered mainly by the low efficiency of injection, the inability to obtain sufficiently enriched stem cell population, and the risks of insertional mutagenesis.

8. The improvement in early survival of patients with acute myocardial infarction treated with streptokinase has still not been proven to be associated with a long-term survival benefit.

9. The determination of the frequencies of particular DNA polymorphisms should be established in each population prior to their implementation in the forensic medical practice.

10. Administration of iron derivatives in addition to erythropoietin facilitates the correction of anemia in patients with normal and even increased iron stores.

11. Mild mutations of the CFTR gene can be the cause of infertility in otherwise normal male individuals.

12. Molecular medicine should be included as a separate discipline in the curriculum of the Medical Faculties.

13. The European Economic Community should recognize The Republic of Macedonia under its genuine name.